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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/759,674	01/16/2004	Mohit Trikha	CEN 5016 US NP	8594

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EXAMINER	
HOLLERAN, ANNE L	
ART UNIT	**PAPER NUMBER**
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/759,674	TRIKHA ET AL.	
	Examiner	Art Unit	
	Anne L. Holleran	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1-14 and 16, drawn to methods of treating proliferative diseases comprising co-administering a steroid in combination with an IL-6 antagonist, classified in class 424, subclass 130.1.

   II. Claims 15 and 16, drawn to methods of treating cerebral edema comprising administering to a mammal a corticosteroid in combination with an IL-6 antagonist, classified in class 424, subclass 130.1.

2. The inventions are distinct, each from the other, for the following reasons:

Inventions I and II are directed to related processes. The related inventions are distinct if the (1) the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect; (2) the inventions do not overlap in scope, i.e., are mutually exclusive; and (3) the inventions as claimed are not obvious variants. See MPEP § 806.05(j). In the instant case, the inventions as claimed are distinct, because Invention I is directed to the treatment of proliferative diseases such as cancer, whereas Invention II is directed to the treatment of cerebral edema. Proliferative diseases such as cancer are distinct from cerebral edema, and the treatment of the two types of disease states comprises treating separate populations of patients, and the observation of different effects and functions of the agents used to treat the diseases. In one case, the use of the agents must result in destruction of tumor tissue, whereas in the other case the use of the agents must result in the decrease of

vascular permeability of blood vessels. Furthermore, the inventions as claimed do not encompass overlapping subject matter and there is nothing of record to show them to be obvious variants.

Additionally, it would place an undue burden on the examiner to have to search and examine the two distinct groups together because the searches and examination would not be coextensive, because proliferative diseases are distinct from cerebral edema and because the mechanism by which the agents would induce their effects for the purpose of treating the two types of diseases would require different searches and considerations.

Because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art due to their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

This application contains claims directed to the following patentably distinct species: species of proliferative diseases:

a) cancer and metastasis

b) seborrheic dermatitis and acne

c) arthritis

The species are independent or distinct because cancer and metastasis involves a dysregulation of growth of cells, whereas seborrheic dermatitis and acne involves the overgrowth of microorganisms and the skin's response to that overgrowth, whereas, arthritis encompasses autoimmune processes. Therefore, each species is a separate and distinct subgenus of proliferative disease.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, 1-11 and 16 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

During a telephone conversation with Ken Dow on 7/12/2006 a provisional election without traverse to prosecute the invention of Group I, species of cancer and metastasis, claims 1-14 and 16. Affirmation of this election must be made by applicant in replying to this Office action. Claim 15 and 16(to the extent to which is dependent on claim 15) are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

3. Claims 1-16 are pending. Claims 15 and 16 (to the extent that it depends from 15), drawn to non-elected inventions, are withdrawn from consideration.

Claim Rejections - 35 USC § 112

4. Claims 1-14 and 16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating proliferative diseases comprising administering a corticosteroid such as dexamethasone in combination with an anti-IL-6 antibody that neutralizes the angiogenic effects of IL-6, does not reasonably provide enablement for methods of treating proliferative diseases comprising administering any steroid in combination with any IL-6 antagonist. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification has not provides sufficient guidance for using any steroid other than a corticosteroid for the treatment of proliferative diseases. The specification has not provided sufficient guidance for using any IL-6 antagonist for the treatment of proliferative diseases, because the specification fails to teach how to make a sufficient number of IL-6 antagonists.

Claims 1-12 (and 16, in part) are drawn to methods comprising the administration of a steroid in combination with an IL-6 antagonist. The intended use of the claimed methods is the treatment of proliferative diseases amenable to treatment by an apoptosis inducing agent; the inhibition of tumor growth in a mammal; or the prevention of metastasis in a mammal. The term "steroid" encompasses compounds that would not have the effect of inducing apoptosis in a proliferative disease state. For example, in breast cancer, a steroid such as estrogen promotes

growth of the cancer instead of promoting apoptosis. Similarly, in prostate cancer, a steroid such as testosterone promotes the growth of cancer instead of promoting apoptosis. Therefore, it does not appear that the specification provides adequate guidance for the use of any steroid in a method for the treatment of a proliferative disease, where the purpose of the method is to induce apoptosis.

Claims 1-14 and 16 encompass methods that comprise administration of a steroid (claims 1-12, 16) or a corticosteroid (claims 13, 14, 16) in combination with an IL-6 antagonist that is an antibody, fragment thereof, or an anti-IL-6 antibody or fragment thereof. The specification defines IL-6 antagonist on page 11, lines 10-11, as a substance that inhibits or neutralizes the angiogenic activity of IL-6. The specification further suggests possible chemical structures of products that may be used as IL-6 antagonists, such as anti-IL-6 antibodies that bind to IL-6 with sufficient affinity and specificity to neutralize the angiogenic effect of IL-6. However, the claims encompass methods using fragments of antibodies, where the structure of the fragment, (or the antibody from which the fragment is derived) is not specified.

The specification teaches a few examples of useful anti-IL-6 antibodies, such as cCLB8 and BE-8. However, the prior art teaches that not all anti-IL-6 antibodies would be useful in neutralizing IL-6 activity and that some antibodies are not capable of neutralizing IL-6 activity (see Brakenhoff, J.P.J., Journal of Immunology, 145: 561-568, 1990; page 561, 2nd column, and page 564, 1st and 2nd col., bridging paragraph). Furthermore, it is well established in the art that the formation of an intact antigen-binding site generally requires the association of the complete heavy and light chain variable regions of a given antibody, each of which consists of three CDRs which provide the majority of the contact residues for the binding of the antibody to its target

epitope. The amino acid sequences and conformations of each of the heavy and light chain CDRs are critical in maintaining the antigen binding specificity and affinity of the parent immunoglobulin. It is expected that all of the heavy and light chain CDRs in their proper order and in the context of framework sequences, which maintain their required conformation, are required in order to produce a protein having antigen-binding function; and that proper association of heavy and light chain variable regions is required in order to form functional antigen binding sites. Even minor changes in the amino acid sequences of the heavy and light variable regions, particularly in the CDRs, may dramatically affect antigen-binding function as evidenced by Rudikoff et al (Proc Natl Acad Sci USA 1982 Vol 79 page 1979). Rudikoff et al. teach that the alteration of a single amino acid in the CDR of a phosphocholine-binding myeloma protein resulted in the loss of antigen-binding function. Because the claims recite "fragments" of antibodies without specifying the antibody from which the fragment was derived, and also without specifying the molecular nature of the fragment, and because the term "fragment" encompasses something as small as one amino acid of an antibody, the claims broadly encompass fragments which may contain less than the full complement of CDRs from the heavy and light chain variable regions of a useful anti-IL-6 antibody. Therefore, a large portion of the genus of "fragments" of antibodies would not have the required binding and neutralizing function required for the operation of the claimed methods. Thus, further experimentation would be required by one of skill in the art to discover antibody fragments that would be useful as IL-6 antagonists, and that have the specific activity discussed in the specification of inhibiting or neutralizing the angiogenic activity of IL-6. Therefore, undue experimentation would be required to make methods encompassed by the claims.

5. Claims 5 and 16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not set forth in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 5 is drawn to a method using an antibody that competes for binding with monoclonal antibody cCLB8 for binding to human IL6. Therefore, the claim requires cCLB8 to test for an antibody that competes for binding. Claim 16 is drawn to a method comprising the use of the specific antibody cCLB8, which is the chimeric version of CLB8. The specification fails to describe how to make the cCLB8 monoclonal antibody. Furthermore, the specification fails to provide enough information for one of skill in the art to produce a monoclonal antibody with exactly the same characteristics as the cCLB8 monoclonal antibody. Even if the specification did provide enough information for one of skill in the art to produce a monoclonal antibody with properties similar to those of the cCLB8 monoclonal antibody, reproduction of an identical monoclonal antibody is an unpredictable event. Because it does not appear that the cCLB8 monoclonal antibody is publicly available or can be reproducibly isolated from nature without undue experimentation, one of ordinary skill in the art cannot be assured of the ability to practice the claimed inventions. Because claims 5 and 16 specifically require the use of the cCLB8 monoclonal antibody, a suitable deposit of the hybridoma producing the cCLB8 monoclonal antibody is required, or evidence must be provided that the cCLB8 monoclonal antibody is well known and readily available to the public, or that it is reproducible without undue experimentation.

Furthermore, unless a deposit was made at or before the time of filing, a declaration filed under the 37 C.F.R. 1.132 is necessary to construct a chain of custody. The declaration, executed by a person in a position to know, should identify the deposited hybridoma by its depository accession number, establish that the deposited hybridoma is the same as that described in the specification, and establish that the deposited hybridoma was in applicant's possession at the time of filing. Applicant is required to amend the specification to recite the accession number of the deposit, the date of deposit, a description of the deposited biological material, and the name and address of the depository. See In re Lundak, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

If the deposit is made under the provision of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposits have been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the Budapest Treaty as the treaty leaves this specific matter to the discretion of each member state.

If the deposits are not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an

attorney of record who has the authority and control over the conditions of deposit, over his or her signature and registration number, averring:

(a) that all restrictions on the availability to the public of the material will be irrevocably removed upon the granting of a patent.

(b) that the material has been deposited under conditions that ensure that access to the material will be available during the pendancy of the patent application to one determined by the Commissioner to be entitled thereto under 35 CFR 1.14 and 35 USC 122.

(c) that the deposited material will be stored with all care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case at least thirty (30) years after the date of a deposit or for the enforceable life of the patent, whichever is longer.

(d) that the duty to replace the deposit should the depository be unable to furnish a sample when requested due to the condition of the deposit.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this

subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-7, 9-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Morreau (British Journal of Haematology 109: 661-664, 2000) as evidenced by Kalai (Kalai, M. et al. European Journal of Biochemistry, 249: 690-700, 1997).

Morreau teaches a method of treating multiple myeloma in human patients, where the method comprises infusing a total of 250 mg of BE-8 (an anti-IL-6 murine Ab) over a period of 4 days in combination with 40 mg/day of dexamethasone (DXM) followed by administration of melphalen (HDM220) and autologous stem cell transfusion (ASCT) (see Morreau, page 661-662). The treatment resulted in complete response in some patients (see Table 1, page 662). Thus, Morreau teaches a method of treating a proliferative disease, and in prevention of metastasis.

BE-8 is an anti-IL-6 antibody that binds to an epitope that overlaps with the epitope on IL-6 that is bound by CLB8 antibody (see Kalai, pages 691, 1st column "Antibodies"; page 694, 1st column, 2nd full paragraph, and page 698, 1st column). Thus, Morreau teaches a method comprising the administration of an antibody that competes with antibody cCLB8 for binding to human IL6.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1, 9, 10, 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brakenhoff (US Patent 5,723,120; issued 03/1998) in view of Morreau (supra).

Claims 1, 9, 10, 11 and 12 encompass the use of IL-6 antagonists that are not anti-IL-6 antibodies.

Brakenhoff teaches methods of treating multiple myeloma comprising the administration of an IL-6 antagonist that is a mutated IL-6 polypeptide comprising amino acids 30-185 of mature IL-6 protein having mutations in the region corresponding to amino acid positions 154

through 163 of mature IL-6 protein, where the mutations decrease IL-6 signal transduction activity relative to IL-6 receptor-binding activity.

Brakenhoff fails to teach the method comprising the coadministration of a steroid.

However, Morreau teaches a method of administering dexamethasone in combination with an anti-IL-6 antibody for the treatment of multiple myeloma. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified Brakenhoff's method to include the coadministration of dexamethasone in the treatment of multiple myeloma. One of skill in the art would have been motivated to include dexamethasone in a method of treating multiple myeloma, because Morreau teaches that dexamethasone is an apoptosis inducing agent and is useful in the treatment of multiple myeloma.

8. Claims 1, 2 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morreau (supra).

Claims 1, 2 and 8 include within their scope methods where the anti-IL-6 antibody is administered in a bolus dose followed by infusion of the antibody.

Morreau teaches infusion of an anti-IL-6 antibody, where on the first day 100 mg is infused over 2 hour, and then on days 2-4, 50mg/day is infused. Morreau fails to teach administration of a bolus dose followed by an infusion. However, the differences between the claimed method and the prior art method appears to be one of optimization of conditions of administration. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have optimized the administration conditions of Morreau to

arrive at the administration conditions recited in the claims. See MPEP 2144.05: A. Optimization Within Prior Art Conditions or Through Routine Experimentation

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

9. Claims 1, 11-14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morreau (British Journal of Haematology 109: 661-664, 2000) in view of Kalai (Kalai, M. et al. European Journal of Biochemistry, 249: 690-700, 1997) and further in view of either van Zaanen-#1 (van Zaanen, H.C.T. et al., British Journal of Haematology, 102: 783-790, 1998) or van Zaanen-#2 (van Zaanen, H.C.T. et al., Journal of Clinical Oncology, 98(6): 1441-1448, 1996).

Claims 1, 11-14 and 16 include within their scope methods comprising the administration of chimeric CLB-8 (cCLB8, also referred to as chimeric CLB IL6/8) antibody in combination with a steroid, such as dexamethasone.

Morreau teaches a method of treating multiple myeloma comprising administering a muriine anti-IL6 antibody, BE-8, in combination with dexamethasone to human patients diagnosed with mutitple myeloma. Morreau fails to teach methods using the specific antibody cCLB8.

However, Kalai teaches that the BE-8 antibody and the CLB.IL6-8 antibody bind to the same region of IL-6. Therefore, these two antibodies appear to be functionally equivalent. Further, van Zaanen-#1 or van Zaanen-#2 teach the use of chimeric CLB IL6/8 antibody for the treatment of human patients suffering from multiple myeloma. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the chimeric CLB IL6/8 antibody (cCLB8) of either van Zaanen-#1 or van Zaanen-#2 in the method of Morreau to make a method for the purpose of treating multiple myeloma comprising the step of administering to a human patient a combination of the cCLB8 anti-IL-6 antibody in combination with dexamethasone. One would have been motivated to have used the chimeric

antibody of either van Zaanen-#1 or van Zaanen-#2 instead of the murine BE-8 antibody, because human patients will have a reduced HAMA response to a chimeric antibody compared to the response to a murine antibody (see van Zaanen-#1, page 783, 2nd col.; van Zaanen-#2, page 1441, 2nd col.).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne Holleran, whose telephone number is (571) 272-0833. The examiner can normally be reached on Monday through Friday from 9:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, can be reached on (571) 272-0832. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Official Fax number for Group 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Anne L. Holleran
Patent Examiner
September 14, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER